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10/591,843	10/18/2007	Tomoaki Hoshino	KUP-12	3086
20/808	7/590	04/12/2012		
BROWN & MICHAELS, PC 400 M & T BANK BUILDING 118 NORTH TIOGA ST ITHACA, NY 14850			EXAMINER SEHARASEYON, JEGATHEESAN	
			ART UNIT	PAPER NUMBER
			1646	
			NOTIFICATION DATE	DELIVERY MODE
			04/12/2012	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary**Application No.**

10/591,843

Applicant(s)

HOSHINO ET AL.

ExaminerJEGATHEESAN
SEHARASEYON**Art Unit**

1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 February 2012.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on ____; the restriction requirement and election have been incorporated into this action.
- 4) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 5) ☒ Claim(s) 1 is/are pending in the application.
- 5a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 6) ☐ Claim(s) ____ is/are allowed.
- 7) ☒ Claim(s) 1 is/are rejected.
- 8) ☐ Claim(s) ____ is/are objected to.
- 9) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 10) ☐ The specification is objected to by the Examiner.
- 11) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 12) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date ____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date ____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: ____

DETAILED ACTION

1. This Office Action is in response to Applicant's amendments and remarks filed 2/6/12. Claim 1 is pending and examined.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2a. The rejection of claim 1 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is maintained for reasons set forth in the Officer Action dated 8/8/11. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim is drawn to a protease inhibitor comprising: a redox activity protein, wherein the protease is selected from the group consisting of MMP-1 and MMP-9, wherein an active site of the redox activity protein has -Cys-X1-X2-Cys, where X1 and X2 are amino acid residues.

The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. See *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404. The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (1) the breadth of the claims; (2) the nature of the

invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by the inventor; (7) the existence of working examples; and (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

In arguing that the specification is enabling for an inhibitor of at least one protease comprising a redox activity protein, wherein the protease is selected from the group consisting of MMP-1 and MMP-9, wherein an active site of the redox activity protein has –Cys-X1-X2-Cys, where X1 and X2 are amino acid residues, Applicant questions the findings of Farina et al. and Sahlin et al. Specifically, Applicant contends that Farina et al. reference cannot show precise quantification because MMP-9 activity is not directly determined. Further, Applicant appears to also cast doubt on the findings of Sahlin et al. reference because it does not show any data. Applicant also is arguing that since the instant Application includes working examples, there is strong evidence that undue experimentation would not be required in order to practice the invention (Applicant restated the experimental data starting on page 30).

Applicant's arguments have been fully considered but are not found to be persuasive. In the instant application claims are broadly drawn to an inhibitor of at least one protease comprising a redox activity protein, wherein the protease is selected from the group consisting of MMP-1 and MMP-9, wherein an active site of the redox activity protein has –Cys-X1-X2-Cys, where X1 and X2 are amino acid residues. Thus, the claim as described is not limited to Thioredoxin (TRX). Although, the specification on page 30 asserts that TRX has inhibitory effect with respect to protease such as cysteine

protease and metalloprotease, Farina et al. (2001) and Sahlin et al. (2000) references at least partially contradict Applicant's assertion. Farina et al. for example state that TRX does not inhibit MMP-9 activity (abstract and page 410, right column 2nd paragraph, lines 18-21). In addition, Sahlin et al. on page 1151 (see Figure 4 and column 2) teach away from instant invention in that TRX and glutaredoxin by inactivating tissue inhibitors (TIMP-1 and TIMP-2) of metalloproteinases (MMP) by disulphide reduction may promote MMP-2 and MMP-9 activity involved in collagen breakdown. Although, Applicant questions the findings of Farina et al. and Sahlin et al., they have not provided independent evidence to refute the finding of Farina et al. and Sahlin et al. Therefore, given the breadth of claim an inhibitor of at least one protease comprising a redox activity protein, wherein the protease is selected from the group consisting of MMP-1 and MMP-9, wherein an active site of the redox activity protein has -Cys-X1-X2-Cys, where X1 and X2 are amino acid residues, the state of the prior, along with the level of predictability and the lack of working examples (applicant has only disclosed TRX).

Therefore, undue experimentation would be required to practice the claimed invention with a reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to effectively practice the claimed invention and absent working examples providing evidence which is reasonably predictive that the claimed invention is effective for identifying a protease inhibitor comprising: a redox activity protein, wherein the protease is selected from the group consisting of MMP-1 and MMP-9.

Claim Rejections - 35 USC § 112 (written description, New)

2b. Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claim recites

a protease inhibitor comprising: a redox activity protein, wherein the protease is selected from the group consisting of MMP-1 and MMP-9, wherein an active site of the redox activity protein has –Cys-X1-X2-Cys, where X1 and X2 are amino acid residues.

The specification discloses Thioredoxin (TRX) an inhibitor of at least one protease disclosed in the claim. This meets the written description provisions of 35 USC 112, first paragraph. However, the specification does not disclose all possible inhibitor of at least one protease comprising: a redox activity protein, wherein the protease is selected from the group consisting of MMP-1 and MMP-9, wherein an active site of the redox activity protein has –Cys-X1-X2-Cys, where X1 and X2 are amino acid residues contemplated by the Applicant.

The claims as written, however, encompass inhibitor of at least one protease comprising: a redox activity protein, wherein the protease is selected from the group consisting of MMP-1 and MMP-9, wherein an active site of the redox activity protein has

–Cys-X1-X2-Cys, where X1 and X2 are amino acid residues which were not originally contemplated and fail to meet the written description provision of 35 USC 112, first paragraph because the written description is not commensurate in scope with the recitation of claim 1. The specification does not provide written description to support the genus encompassed by the instant claims.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the ‘written description’ inquiry, whatever is now claimed.” (See page 1117.) The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed” (See *Vas-Cath* at page 1116).

With the exception of TRX an inhibitor of at least one protease, the specification as filed fails to disclose any other inhibitors of protease contemplated in the instant claim. Thus, the skilled artisan cannot envision all the detailed chemical structure of the claimed inhibitor of at least one protease comprising: a redox activity protein, wherein the protease is selected from the group consisting of MMP-1 and MMP-9, wherein an active site of the redox activity protein has –Cys-X1-X2-Cys, where X1 and X2 are amino acid residues regardless of the complexity or simplicity of the method of isolation.

Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The polypeptide itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes v. Baird*, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class.

Therefore, only the inhibitor of at least one protease TRX, but not the full breadth of the claims meets the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the

genus is highly variant. As a result, it does not appear that the inventors were in possession of various polynucleotide sequences set forth in claims 1.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.) Applicants are directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 64, No. 244, pages 71427-71440, Tuesday December 21, 1999.

Claim Rejections - 35 USC § 102 (reinstated)

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3a. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Farina et al. (2001, IDS of 6/25/08).

Claim(s) is drawn to a protease inhibitor protein with redox activity. Farina et al discloses Thioredoxin (TRX) a redox enzyme (protein) which is a protease inhibitor. Thioredoxin inhibits metalloproteinases and other proteases. In addition, Farina teaching that redox enzyme Thioredoxin (TRX) contains a highly conserved Cys-Gly-Pro-Cys active site. It is also noted that a compound and all its properties are inseparable. See also In re Papesch, 315 F.2d 381, 391, 137 USPQ 43, 51 (CCPA

1963) ("From the standpoint of patent law, a compound and all its properties are inseparable.") Therefore, Farina et al. anticipates the instant invention.

Response to Applicant's Remarks

3b. Applicant's asserts that Farina et al. does not disclose, teach, suggest the use of MMP-1, nor does the Examiner provide any support or evidence that MMP-2 would have the same protease activity and/or function, or that MMP-2 is a substitute for MMP-1. Additionally, Farina et al. teaches away from an inhibitor of MMP-9. Applicant's arguments have been fully considered but are not found to persuasive because claims are drawn to a composition comprising an inhibitor of at least one protease which is redox activity. In addition, Farina teaching that redox enzyme Thioredoxin (TRX) contains a highly conserved Cys-Gly-Pro-Cys active site. See also In re Papesch, 315 F.2d 381, 391, 137 USPQ 43, 51 (CCPA 1963) ("From the standpoint of patent law, a compound and all its properties are inseparable."). Therefore Farina et al. teaches the limitation(s) of the instant claim.

Conclusion

4. No claims are allowed.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JEGATHEESAN SEHARASEYON whose telephone number is (571)272-0892. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Vanessa L. Ford can be reached on 571-272-0857. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

JS
4/5/12
/Jegatheesan Seharaseyon/
Examiner, Art Unit 1646